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JOHN S. PRATT, ESQ
KILPATRICK STOCKTON, LLP
1100 PEACHTREE STREET
SUITE 2800
ATLANTA, GA 30309

[REDACTED] EXAMINER

ANGELL, JON E

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1635

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Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|----------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/857,332 | PHILLIPS ET AL. |
| | Examiner J. Eric Angell | Art Unit 1635 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on ____.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 33-64 is/are pending in the application.

4a) Of the above claim(s) ____ is/are withdrawn from consideration.

5) Claim(s) ____ is/are allowed.

6) Claim(s) 33-64 is/are rejected.

7) Claim(s) ____ is/are objected to.

8) Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on ____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on ____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. ____.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8

4) Interview Summary (PTO-413) Paper No(s). ____

5) Notice of Informal Patent Application (PTO-152)

6) Other: ____

DETAILED ACTION

Claims 33-64 are pending in the application.

Election/Restrictions

Applicant has cancelled all previously filed claims and added new claims 33-64 (amendment B, filed 4/15/02). The previously issued restriction requirement is withdrawn in view of the aforementioned amendment.

Claims 33-64 are examined herein.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 33-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33, 41, 49 and 57 are independent claims that are drawn to methods of treating cancer comprising administration of a composition comprising mycobacterium DNA complexed on mycobacterial cell wall and a pharmaceutical acceptable carrier to an animal having cancer; wherein the composition and a chemotherapeutic agent administered to the animal having cancer display an anti-cancer synergism.

The instant claims (an all dependent claims) are indefinite because it is unclear if the method is a treatment comprising the administration of the composition described above and a

pharmaceutically acceptable carrier, or if the method is a treatment comprising the administration of the composition described above, a pharmaceutically acceptable carrier, and a chemotherapeutic agent. It is noted that the claims, as written, only require that the treatment comprises administration of the composition and a pharmaceutically acceptable carrier to the animal. The claims do not require that the treatment comprises administration of the composition, a pharmaceutically acceptable carrier and a chemotherapeutic agent. The phrase, "wherein the composition and a chemotherapeutic agent administered to the animal having cancer display an anti-cancer synergism" is confusing because the chemotherapeutic agent is not a required component of the treatment. Therefore, it is unclear if the treatment comprises or does not comprise administration of a chemotherapeutic agent in addition to the composition and pharmaceutically acceptable carrier.

Amendment of the claims to clearly recite that the treatment comprises administration of a composition comprising administration of a composition comprising mycobacterium DNA complexed on mycobacterial cell wall in a pharmaceutical acceptable carrier and a chemotherapeutic agent to an animal having cancer would obviate this rejection. Alternatively, amendment of the claims to delete the phrase, "wherein the composition and a chemotherapeutic agent administered to the animal having cancer display an anti-cancer synergism" would also obviate this rejection.

Claims 33, 41, 49 and 57 recite the phrase, "wherein the composition and a chemotherapeutic agent administered to the animal having cancer display an anti-cancer synergism". This phrase renders the claims indefinite because the specification defines the term "synergism" as "the coordinated action of two or more chemotherapeutic agents" (see p. 6, line

7-8). However, this definition is vague because it is unclear what constitutes a “coordinated action of two or more chemotherapeutic agents” because the specification does not clearly define “a coordinated action”. For instance, it is unclear if the action is coordinated through a common cellular pathway, or if the action is a coordinated effect such as a similar cellular effect. Two agents that can have a similar cellular effect, such as killing the cell, can work through different pathways such as apoptotic and necrotic cell death pathways.

Claims 34-40, 42-48, 50-56 and 58-63 are dependent claims and are rejected for the same reasons.

Additionally, claims 34, 42, 50, and 58 recite, “wherein the anti-cancer synergism is potentiation”. This phrase is also unclear because the specification defines “potentiates” as, “relates to a degree of synergism that is greater than additive” (see p. 6, line 5-6). Without a clear definition of the term “synergism” the terms “potentiates” and “potentiation” are also unclear and indefinite.

Furthermore, claims 33 and 49 recite the phrase, “a composition comprising a mycobacterial DNA complexed on mycobacterial cell wall (BCC)”. This phrase renders the instant claims (and claims depending on 33 and 49) indefinite because it is unclear how the DNA is complexed on the cell wall. The specification does not explicitly disclose any method steps to complex the mycobacterial DNA to the cell wall (see p. 9, Examples 1 and 2). Therefore it is unclear if any particular methods are required to complex the mycobacterial DNA to the cell wall. It is noted that the mycobacterial cell wall would inherently have DNA complexed to the cell wall. Therefore, any mycobacterial cell wall would inherently have complexed mycobacterial DNA, unless the cell wall is specifically treated with nuclease such as DNase.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 33, 35, 37, 41, 43, 45, 49, 51, 53, 56, 57, 59, 61 and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Morales et al. (J. Urology 153:1706-1710; 1995).

As mentioned above, it is unclear if the claims are drawn to a method comprising administration of a composition and pharmaceutically acceptable carrier or a method comprising administration of a composition in a pharmaceutically acceptable carrier and a chemotherapeutic agent. Therefore, the following rejection is appropriate because there is no explicit requirement that the method comprises administration of the composition, the carrier and the chemotherapeutic agent.

Morales teaches a method of treating cancer comprising administration of a composition comprising mycobacterial DNA from *M. phlei* (see p. 1706, first column) and a pharmaceutically acceptable carrier (here, oil microdroplets; p. 1706 first column) to an animal having cancer in an amount effective to have an antineoplastic effect (i.e. inhibition of proliferation of cancer cells) on the tumor in the animal having the cancer (see abstract, Fig. 2), wherein the tumor cells are resistant to a chemotherapeutic agent, here BCG (see p. 1706, first paragraph of second column); the *M. phlei* DNA is preserved and complexed to the cell wall because the cell wall would

inherently have the cell's DNA preserved and complexed to the cell wall unless the cell wall was specifically treated to remove the DNA with agents such as nucleases.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 33, 35-37, 41, 43-45, 49, 51-53, 56, 57, 59-61 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morales et al. (J. Urology 153:1706-1710; 1995) in view of Filion et al. (Blood, Vol 90, No. 10, Suppl 1 (part 1 of 2); p. 168b, abstract 3476; Nov. 1997) and further in view of Filion et al. (Blood, Vol 90, No. 10, Suppl 1 (part 1 of 2); p. 58b, abstract 2959; Nov. 1997).

As mentioned above, it is unclear if the claims are drawn to a method comprising administration of a composition and pharmaceutically acceptable carrier or a method comprising administration of a composition in a pharmaceutically acceptable carrier and a chemotherapeutic agent. Therefore, the following rejection is appropriate because there is no explicit requirement that the method comprises administration of the composition, the carrier and the chemotherapeutic agent.

Morales teaches a method of treating cancer comprising administration of a composition comprising mycobacterial DNA from *M. phlei* (see p. 1706, first column) and a pharmaceutically acceptable carrier (here, oil microdroplets; p. 1706 first column) to an animal having cancer in an amount effective to have an antineoplastic effect (i.e. inhibition of proliferation of cancer cells) on the tumor in the animal having the cancer (see abstract, Fig. 2), wherein the tumor cells are resistant to a chemotherapeutic agent, here BCG (see p.1706, first paragraph of second column); the *M. phlei* DNA is preserved and complexed to the cell wall because the cell wall would inherently have the cell's DNA preserved and complexed to the cell wall unless the cell wall was specifically treated to remove the DNA with agents such as nucleases.

Morales does not teach that the composition induces apoptosis in cells of the cancer, or that the cancer is leukemia.

Filion (abstract 3476) teaches that *M. phlei* DNA has a direct anti-tumor effect on leukemic cells in vitro by inducing apoptosis (see title and last three lines of abstract). Filion (abstract 3476) also teaches that the *M. phlei* DNA treatment induces IL-12 in vitro, which was known to activate apoptosis (see abstract).

Filion (abstract 3476) does not teach that the *M. phlei* DNA is complexed to cell mycobacterial cell wall, or that the DNA is administered to an animal.

Filion (abstract 2959) teaches that *M. phlei* cell wall complex comprising *M. phlei* DNA induces IL-12 synthesis when injected into mice (see abstract, lines 7-10). Filion (abstract 2959) also teaches, "the IL-12 synthesized in response to this DNA may be in part responsible for the anti-tumor activity of *M. phlei* MCC" (see last two line of abstract).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Morales, Filion (abstract 3476) and Filion (abstract 2959) and devise a method to treat cancer wherein Mycobacterial cell wall complex comprising *M. phlei* DNA is administered to an animal having cancer (as taught by Morales), wherein the cancer is leukemia, and wherein treatment activates apoptosis in the leukemic cells (as taught by Filion, abstract 3476) with a reasonable expectation of success. The expectation of success is evidenced by Morales teachings that *M. phlei* cell wall complex has an anti-tumor effect in mice, Filion (abstract 3476) teachings that *M. phlei* DNA activates apoptosis of leukemic cells *in vitro* possibly through IL-12 induction, and Filion (abstract 2959) teachings that mycobacterial cell wall complex comprising *M. phlei* DNA induces IL-12 synthesis in mice.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell
May 15, 2002


JEFFREY FREDMAN
PRIMARY EXAMINER